P1101: PHASE II STUDY OF RALTGRAVIR CONTAINING REGIMEN IN HIV-TH-BC TREATED CHILDREN AGED 6 TO <12 YEARS

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Background: Current antiretroviral (ARV) treatment options for HIV-infected children with TB disease are limited. Raltegravir (RAL) induces UDP-glucuronosyltransferase activity, accelerating the clearance of raltegravir (RAL). In adults, doubling the RAL dose partially overcomes this pharmacokinetic (PK) interaction without safety concerns, but it is not clear if this will be effective in children. To determine whether doubling the dose of RAL for HIV-infected children receiving RIF-containing anti-TB therapy is safe and feasible in children, we conducted a phase III study.

Methods: P1101 is a phase III dose finding study for RAL in HIV-infected children receiving Rif-containing anti-TB therapy for at least one week, with three age cohorts: Cohort 1: 2 to <6 years (closed), Cohort 2: 6 to <12 years of age (closed) and Cohort 3: 3 years to <2 years, aiming to enroll 12 evaluable participants for PK and safety in each cohort. At enrollment participants start 3 ARVs, including chewable RAL formulation at 12 mg/kg/dose twice daily (twice the recommended pediatric dose). Intensive RAL PK sampling is done 1 week after ARV therapy is initiated and then a 4th ARV (standard of care with treatment) is added, usually efavirenz (EFV) or lopinavir/ritonavir (LPV/r). Clinical and laboratory assessments are routinely completed. RAL is stopped at treatment completion and participants are followed for an additional 3 months. PK targets are geometric mean (GM) AUC(12h) of 14 \(\mu\)g/mL (CV = 45%), median C12h of 17.2 \(\mu\)g/mL (IQR: 14.5 - 20.4 \(\mu\)g/mL), and GM C12h ≥75 nM. (CV = Standard deviation/mean) are calculated. All adverse events related to RAL were reported. 12/14 had evaluable efficacy data at week 8 (2/14 discontinued RAL prior to the completion of intensive pharmacokinetic study for RAL).

Observations: Double the dose of RAL for TB-HIV co-infected children 6 to <12 years of age while taking rifampicin achieved adequate PK levels. A dose of 12 mg RAL appeared to achieve viral suppression as part of combination antiretroviral treatment for TB-HIV co-infected children taking rifampicin in this age group.

Conclusions: The study team would like to thank the P1101 participants and families for their participation.

References